REMARKS

Claims 1-33 have been rejected, while claims 34 and 35 have been withdrawn from consideration. Claims 2, 16, 34 and 35 have been cancelled herein without prejudice, and claims 36-41 have been added. Thus, claims 1, 3-15, 17-33, and 36-41 are pending.

The specification has been amended to change the "DESCRIPTION OF DRAWINGS" heading to "BRIEF DESCRIPTION OF THE DRAWINGS" as suggested by the Examiner.

In addition, claims 1, 4, 8, 9, 13, 19, 23, and 24 have been amended. In particular, claims 1 and 13 have been amended to indicate (1) that the arthritis condition is a rheumatoid arthritis condition, (2) that the marker is an elevated level of a CD21L polypeptide, an elevated level of a lymphotoxin-α polypeptide, an elevated level of a lymphotoxin-β polypeptide, an elevated level of an SLC polypeptide, an elevated level of a DC-CK 1 polypeptide, an elevated level of an MCP-1 polypeptide, or an elevated level of a BLC polypeptide, and (3) that the sample comprises synovial tissue or synovial fluid. Claims 4 and 19 have been amended to indicate that the sample is a synovial fluid sample. Claims 8 and 23 have been amended to indicate that the at least one marker is the elevated level of a BLC polypeptide. Claims 9 and 24 have been amended to indicate that the at least one marker is the elevated level of a lymphotoxin-α polypeptide. New claims 36 and 39 indicate that the at least one marker is the elevated level of an SLC polypeptide. New claims 37 and 40 indicate that the at least one marker is the elevated level of a DC-CK 1 polypeptide. New claims 38 and 41 indicate that the at least one marker is the elevated level of a MCP-1 polypeptide.

Applicants' specification fully supports these claim amendments and new claims. For example, page 15, lines 25-26 disclose that LT-α, LT-β, BLC, SLC, DC-CK 1, and MCP-1 are predictive of GC^+ follicles, while page 9, lines 18-20 disclose that the sample can be synovial tissue or synovial fluid. Thus, no new matter has been added.

According to the Examiner's comments in the detailed action, it appears that the entire scope of original claims 1-33 were searched and examined despite the species election. Thus, Applicants' comments are in response to the full scope of the presently amended claims. In light

of this and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1, 3-15, 17-33, and 36-41.

Objection to Specification

The Examiner objected to the specification stating that Applicants are required to use the heading "Brief Description of the Drawings" to describe the drawings. The specification has been amended to change the "DESCRIPTION OF DRAWINGS" heading to "BRIEF DESCRIPTION OF THE DRAWINGS" as suggested by the Examiner. In light of the above, Applicants respectfully request withdrawal of the objection to the specification.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1, 8, 13, and 23 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that it is not clear what a chemoattractant polypeptide is and that this term provides no information as to the structure of the polypeptide.

Applicants respectfully disagree. A person having ordinary skill in the art at the time Applicants filed would have understood the meaning of original claims 1, 8, 13, and 23. To further prosecution, however, claims 1, 8, 13, and 23 have been amended to recite a BLC polypeptide as opposed to a chemoattractant polypeptide. A person having ordinary skill in the art at the time Applicants filed would have understood the meaning of a BLC polypeptide, especially given Applicants' disclosure, e.g., in Example 3 starting on page 12. In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 8, 13, and 23 under 35 U.S.C. § 112, second paragraph.

The Examiner also rejected claims 9 and 24 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that it is not clear what a

B-chemoattractant polypeptide is and that this term provides no information as to the structure of the polypeptide.

Applicants note that original claims 9 and 24 recited a B-lymphocyte chemoattractant polypeptide as opposed to a B-chemoattractant polypeptide. As pointed out above, a person having ordinary skill in the art at the time Applicants filed would have understood the meaning of a B-lymphocyte chemoattractant polypeptide, especially in light of Applicants' disclosure. Nevertheless, claims 9 and 24 have been amended herein to recite a lymphotoxin-α polypeptide.

In light of these amendments, Applicants respectfully request withdrawal of the rejection of claims 9 and 24 under 35 U.S.C. § 112, second paragraph.

The Examiner rejected claims 12, 32, and 33 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that these claims lack sufficient antecedent basis.

Applicants respectfully disagree. Nevertheless, independent claims 1 and 13 have been amended herein to indicate that the marker is an elevated level of a CD21L polypeptide, an elevated level of a lymphotoxin-α polypeptide, an elevated level of a lymphotoxin-β polypeptide, an elevated level of an SLC polypeptide, an elevated level of a DC-CK 1 polypeptide, an elevated level of an MCP-1 polypeptide, or an elevated level of a BLC polypeptide. Thus, dependent claims 12, 32, and 33 have proper antecedent basis.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 12, 32, and 33 under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-33 under 35 U.S.C. § 112, first paragraph, because:

> the specification, while being enabling for determining the severity of a rheumatoid arthritis (RA) condition in a mammal, said method comprising determining whether or not a sample of synovial tissue from said mammal contains at least one marker, said marker being an elevated level of CD2IL polypeptide, lymphotoxin α (LT-α), lymphotoxin β (LT-β), B-lymphocyte

chemoattractant (BLC), secondary lymphoid tissue cytokine (SLC), dendritic cell-derived C-C chemokine (DC-CK 1) or macrophage chemoattractant protein-1 (MCP-1) and those markers in the prior art that are elevated in RA, wherein the presence of said at least one marker indicates that said arthritis condition is severe, does not reasonably provide enablement for use of other markers to indicate that said arthritis condition is severe.

Applicants respectfully disagree. A person having ordinary skill in the art at the time Applicants filed would have been able to make and use the originally claimed invention without undue experimentation. To further prosecution, however, independent claims 1 and 13 have been amended to recite (1) that the arthritis condition is a rheumatoid arthritis condition, (2) that the marker is an elevated level of a CD21L polypeptide, an elevated level of a lymphotoxin-α polypeptide, an elevated level of a lymphotoxin-β polypeptide, an elevated level of an SLC polypeptide, an elevated level of a DC-CK 1 polypeptide, an elevated level of an MCP-1 polypeptide, or an elevated level of a BLC polypeptide, and (3) that the sample comprises synovial tissue or synovial fluid. As the Examiner acknowledged, Applicants' specification enables such claims.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 3-15, and 17-33 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-5, 7-20, and 22-32 under 35 U.S.C. § 103(a) as being unpatentable over Goronzy *et al.* (U.S. Patent No. 6,555,320 B1) in view of Li *et al.* (U.S. Patent No. 6,075,124) and further in view of Karin *et al.* (U.S. Patent No. 6,075,124), Kara *et al.* (U.S. Patent No. 6,088,695) and Coli *et al.* (U.S. Patent No. 6,018,713). Specifically, the Examiner stated that the Li *et al.* reference discloses that MCP-1 levels were found to be significantly higher in synovial fluid from rheumatoid arthritis patients compared to synovial fluid from osteoarthritis patients and that the Karin *et al.* reference discloses the use of cytokines to treat rheumatoid arthritis by inducing formation of antibodies to the cytokines. The Examiner also stated that it would have been prima facie obvious to a person of ordinary skill in the art at the

time the invention was made to use the chemoattractant polypeptides disclosed in the Goronzy *et al.*, Li *et al.*, and Karin *et al.* patents to determine the severity of RA in a mammal. Further, the Examiner stated that the ordinary artisan would have been motivated to measure the levels of IL-4, IL-10, IFN-γ, IL-1β, TNF-α, TBF-1 [sic], MCP-1, MIP-1α, MCO-1, MIP-1β, and RANTES in a mammalian synovial tissue sample because the "prior art teaches that elevation of said markers, either alone or in combination is an indicator of the severity of the RA condition."

Applicants respectfully disagree. At no point does the combination of cited references teach or suggest that a person having ordinary skill in the art should determine the severity of an arthritis condition in a mammal by determining whether or not a sample contains an elevated level of a CD21L polypeptide, an elevated level of a lymphotoxin-β polypeptide, or an elevated level of a chemoattractant polypeptide.

To further prosecution, however, claims 1 and 13 have been amended to indicate that the marker is an elevated level of a CD21L polypeptide, an elevated level of a lymphotoxin-α polypeptide, an elevated level of a lymphotoxin-β polypeptide, an elevated level of an SLC polypeptide, an elevated level of a DC-CK 1 polypeptide, an elevated level of an MCP-1 polypeptide, or an elevated level of a BLC polypeptide. At no point does the combination of cited references teach or suggest that a person having ordinary skill in the art should determine the severity of a rheumatoid arthritis condition in a mammal by determining whether or not a sample contains such markers.

The Goronzy *et al.* reference does not mention CD21L, lymphotoxin-α, lymphotoxin-β, SLC, DC-CK 1, MCP-1, or BLC polypeptides. Likewise, the Kara *et al.* and Coli *et al.* references fail to mention CD21L, lymphotoxin-α, lymphotoxin-β, SLC, DC-CK 1, MCP-1, or BLC polypeptides. The Li *et al.* reference discloses that MCP-1 levels were found to be significantly higher in synovial fluid from rheumatoid arthritis patients compared to synovial fluid from osteoarthritis patients, while the Karin *et al.* reference discloses inducing the formation of antibodies to cytokines and chemokines such as MCP-1 with the hope that the antibodies will neutralize the activity of the endogenous cytokine to treat rheumatoid arthritis. These references, however, fail to provide any information regarding the use of MCP-1 levels to

assess the severity of a rheumatoid arthritis condition as presently claimed. In fact, a person having ordinary skill in the art reading the Li *et al.* and Karin *et al.* references together with the other cited references would not have been motivated to use MCP-1 levels to determine the severity of a rheumatoid arthritis condition. Thus, the combination of cited references does not render the presently amended claims obvious.

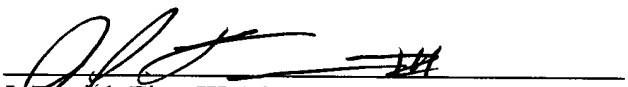
In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 3-5, 7-15, 17-20, and 22-32 under 35 U.S.C. § 103(a).

CONCLUSION

Applicants submit that claims 1, 3-15, 17-33, and 36-41 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. Enclosed is a $36 check for excess claim fees. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: August 27, 2003



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